IBD & Vaccination

A practical guideline for adults with IBD

Rationale :

IBD patients treated with immunomodulators have an increased risk of opportunistic infections and complications.[1]

Vaccination is an effective measure to prevent vaccine-preventable infections and severe complications.

This guideline document aims to clarify the optimal vaccination strategy in the different stages of the disease and in the case of travel.

This guidance document was developed in collaboration with Dr. J-F. Rahier, Prof. Dr. F. Van Gompel and Prof. Dr. T. Moreels.

This guideline is developed based on the most recent ECCO-guidelines:

1: Rahier JF, et al, Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease, J Crohns Colitis (2014), http://dx.doi.org/10.1016/j.crohns.2013.12.013.

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Background :

Vaccine-preventable diseases are a significant source of morbidity and mortality in patients with altered immune competence. IBD patients are considered to be significantly immunocompromised, mainly because of the immunomodulatory medications they take. Routine and specific immunizations are therefore important to consider in this population. Whenever possible, immunization should be considered prior to administering any immunomodulator in order to optimize the immunological response. Prior to foreign travel, IBD patients are best advised by travel medicine specialists familiar with this complex and vulnerable population.[1]

Definition of immunosuppressive therapy[2,3] :

Patients are considered immunosuppressed if treated with any of these drugs:

- Prednisone >20mg/day for >2 weeks
- Azathioprine, 6-mercaptopurine
- Methotrexate
- Anti-TNF therapies, other biologicals
- Ciclosporine, tacrolimus, ...
- Any treatment above, within the past 3 months, except for corticosteroids (within the past month)

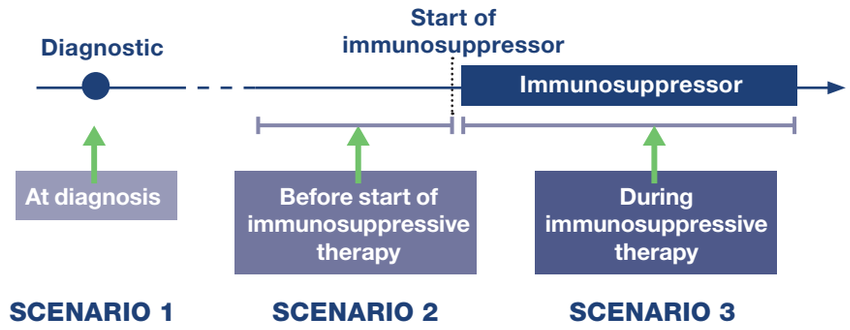
Note :

These treatments are not immunosuppressive:

- 5-ASA
- Prednisone <10mg/day or cumulative dose <700mg[4]
- Beclomethasone dipropionate
- Budesonide ≤ 6mg/day, immunosuppressive characteristic of higher doses is unknown

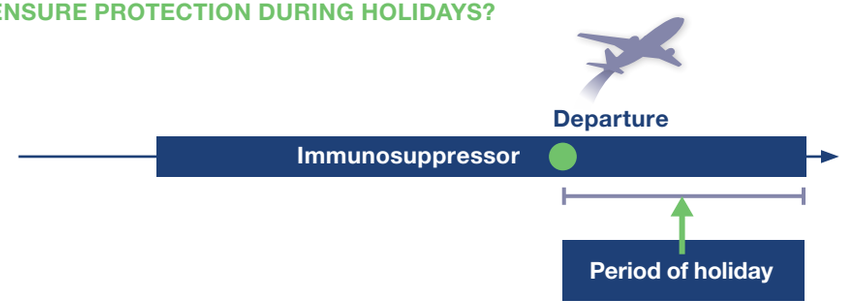
1: Rahier JF, et al. The role of immunization in reducing infections in patients with IBD. IBD Monitor 2009; 9: 106-110.
2: Rahier JF, et al. Vaccinations in patients with immune-mediated inflammatory diseases. Rheumatology 2010; 49: 1815-1827.
3: Belgian Superior Health Council Advisory report 8561 regarding the vaccination of immunocompromised children and adults - 19/10/2011 (http://tinyurl.com/HGR-8561-vacc-immuno = Dutch; http://tinyurl.com/CSS-8561-vacc-immuno = French; http://tinyurl.com/SHC-8561-vacc-immuno =English).
4: Stuck AE, et al. Risk of infectious complications in patients taking glucocorticosteroids. Review of infectious diseases 1989; 11(6): 954-963.

In this document, we consider **3 stages or scenarios** in the course of IBD for the vaccination strategy:



In addition, guidelines for **travel**-specific vaccinations are presented.

WHEN SHOULD THE PATIENT BE VACCINATED TO ENSURE PROTECTION DURING HOLIDAYS?



SCENARIO 1 : What should be done **at diagnosis**?

1. Check with the general practitioners the routine vaccination scheme and immunization history (serologies: HBV, VZV and possibly measles).

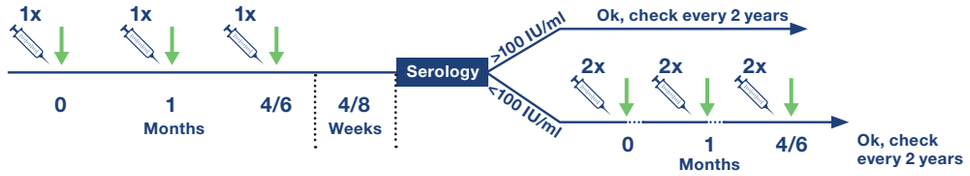
2. Update if necessary:

A) ROUTINE VACCINATIONS (non-live)

- ❍ **Diphtheria** (every 10 years)
- ❍ **Tetanus** (every 10 years)
- ❍ **Pertussis**[1] (one boost in adulthood)
- ❍ **Poliomyelitis** (one boost in adulthood)
- ❍ **Human papilloma virus** (for patient 10-26 years)

B) IBD SPECIFIC NON-LIVE VACCINATIONS

- ❍ **Influenza** (every year for patient > 65 years)
- ❍ **Pneumococcal diseases** (for patient > 65 years)
- ❍ **Hepatitis B**[1] (Engerix B®, HBvaxpro®, Fendrix®, Twinrix®*):
  Serological response should be measured 4 to 8 weeks after the completion of vaccination, and higher doses of immunising antigen may be necessary to achieve success.



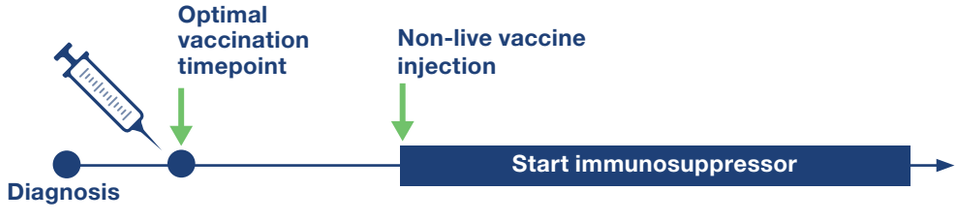
After each double dose booster, consider to measure antibodies, as serological response may already be obtained.

IS IT POSSIBLE TO PERFORM VACCINATION WHILE PATIENT IS UNDER IMMUNOSUPPRESSIVE THERAPY?

SITUATION A AND B: non-live vaccine

There is no contraindication to perform vaccination with non-live vaccine while the patient is under immunosuppressive therapies.

However, for optimal immunization -and if time allows- it is preferable to complete (or at least start) the vaccinations before the start of immunosuppressive therapies.[2]



* Twinrix is a combination vaccine for hepatitis A en B and only contains half a dose of hepatitis A.

1: Belgian Superior Health Council Advisory report 8561 regarding the vaccination of immunocompromised children and adults -19/10/2011 (http://tinyurl.com/HGR-8561-vacc-immuno = Dutch; http://tinyurl.com/CSS-8561-vacc-immuno = French; http://tinyurl.com/SHC-8561-vacc-immuno =English).

2: Peetermans W, et al. Vaccinaties bij immuungecompromitteerde en chronisch zieke patiënten. Tijdschrift voor Geneeskunde 2013; 69: nr. 22, 1113-1116.

C) IBD SPECIFIC LIVE VACCINATIONS

- ❍ **Varicella zoster virus** (Provarivax®, Varilrix®):
  Verify serology if no clear history of:
  - chickenpox or shingles, or
  - varicella zoster virus vaccine

  If the patient is seronegative, immunization should be performed when possible.

- ❍ **Measles, Mumps and Rubella** (M.M.R. VaxPro®, Priorix®):
  Verify serology if no clear history of :
  - measles, or
  - MMR vaccine

  If the patient is seronegative, consider vaccination.

For both vaccinations:

- Consider the risk to be infected and the urgency to start an immunosuppressive therapy.
- Vaccination is at physician's discretion. Attention for patients with high risk contact, e.g. teachers, patients working at a crèche, etc.
- Vaccine is two injections / lifetime, at least 4 weeks apart.

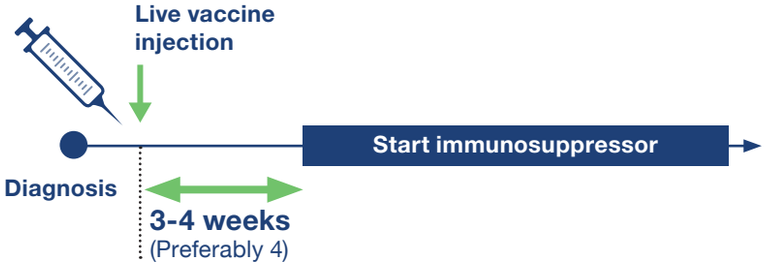
ATTENTION

If patient considers that there is a possibility he/she will ever travel to **yellow fever** endemic regions, please refer to page 10.

IS IT POSSIBLE TO PERFORM VACCINATION WHILE PATIENT IS UNDER IMMUNOSUPPRESSIVE THERAPY?

SITUATION C: Live vaccine[1]

Live vaccine cannot be given when patients are treated with immunosuppressors. Therefore a minimum of 3 weeks delay after the last injection of the live vaccine is necessary before starting immunosuppressive therapies.



For vaccination scheme of patients already under immunosuppressive therapy, refer to scenario 3.

1: Belgian Superior Health Council Advisory report 8561 regarding the vaccination of immunocompromised children and adults - 19/10/2011 (http://tinyurl.com/HGR-8561-vacc-immuno = Dutch;http://tinyurl.com/CSS-8561-vacc-immuno = French;http://tinyurl.com/SHC-8561-vacc-immuno =English).

SCENARIO 2 : What should be done **before start of immunosuppressive therapy**?

In patients that are likely to receive immunosuppressive therapy in the future, update according to scenario 1. Additionally, consider vaccination for:

- **Influenza with inactivated vaccine** (α-Rix®, Agrippal®, Inflexal V®, Influvac S®, Intanza®, Vaxigrip®):
  Vaccinate every year during the seasonal period.
- **Pneumococcal diseases**[1] (Pneumo 23®, Prevenar 13®).

  Pneumococcal disease vaccination scheme for IBD patients:

  For vaccine naive patients:

  For patients that already received Pneumo 23 once*:

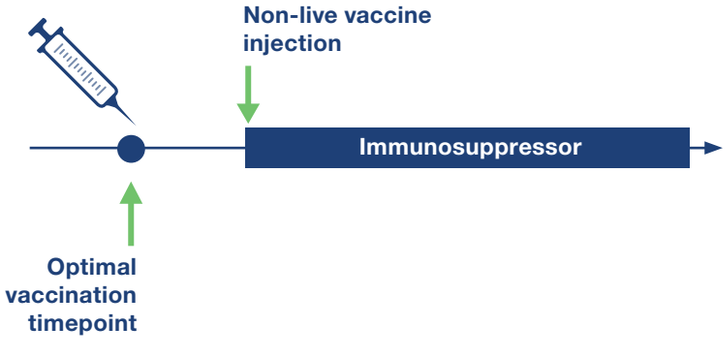
ATTENTION

If patient considers that there is a possibility he/she will ever travel to **yellow fever** endemic regions, please refer to page 10.

IS IT POSSIBLE TO PERFORM VACCINATION WHILE PATIENT IS UNDER IMMUNOSUPPRESSIVE THERAPY?

If immunosuppressive therapy needs to be started immediately, no delay is necessary after the vaccination, and can even be started during the vaccination scheme.

However, for optimal immunization -and if time allows- it is preferable to complete (or at least start) the vaccinations before the start of immunosuppressive therapies.



1: CDC. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2012 Oct 12; 61(40): 816-819.

SCENARIO 3 : What should be done during immunosup pressive therapy?

A) CASE OF NON-LIVE VACCINE

Non-live vaccine can be given to patients on immunosuppressive therapy.
It is not necessary to interrupt the therapy, however efficacy of vaccine may be suboptimal and in some cases booster injections are needed.[1]

Recommendations

The vaccination scheme of immunosuppressed patients should be updated for the following diseases in addition to the other routine vaccinations:

- **Influenza with (seasonal) inactivated vaccine** (α-Rix®, Agrippal®, Inflexal V®, Influvac S®, Intanza®, Vaxigrip®)
- **Pneumococcal diseases** (Pneumo 23®, Prevenar 13®)
- **Hepatitis B** (Engerix B®, HBvaxpro®, Fendrix®, Twinrix®*)
- **Human papilloma virus** (Cervarix®, Gardasil®)

* Twinrix is a combination vaccine for hepatitis A en B and only contains half a dose of hepatitis A.

1: Peetermans W, et al. Vaccinaties bij immuungecompromitteerde en chronisch zieke patiënten. Tijdschrift voor Geneeskunde 2013; 69: nr. 22, 1113-1116.

B) CASE OF LIVE VACCINE

Live vaccines are contraindicated during immunosuppressive therapy.
In Belgium available live vaccines are:

- **Varicella zoster virus** (Provarivax®, Varilrix®)
- **Measles, Mumps and Rubella** (M.M.R. VaxPro®, Priorix®)
- **Yellow fever** (Stamaril®) and **Typhoid fever** (Vivotif®): travel vaccines, refer to page 10.
- **(BCG)**

ATTENTION

If patient considers that there is a possibility he/she will ever travel to **yellow fever** endemic regions, please refer to page 10.

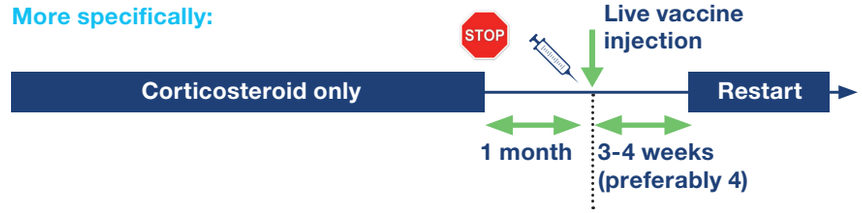
If vaccination with live vaccine is required during immunosuppressive therapy, the therapy must be stopped 3 months before vaccination, and should be withheld for 3 to 4 weeks after live vaccine injection.[1]

Recommended timelines

Overall:

For some immunosuppressive medication, a shorter interval is possible **after consulting an infectious disease/vaccine specialist** (e.g. yellow fever vaccination center)**.**

More specifically:



For corticosteroids, a shorter interval is possible if the dose is lower than the immunosuppressive dose of prednisone >20 mg/day for > 2 weeks. Consult an **infectious disease/vaccine specialist** in such case. If the dose of prednisone is <10mg/day or cumulative dose <700mg it is not considered immunosuppressive and live vaccination can be performed.

1: Peetermans W, et al. Vaccinaties bij immuungecompromitteerde en chronisch zieke patiënten. Tijdschrift voor Geneeskunde 2013; 69: nr. 22, 1113-1116.

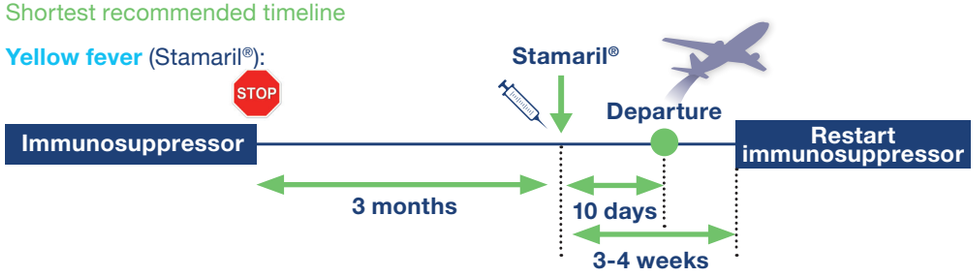
Recommended vaccinations for travel-specific countries can be found on the ITG website: www.itg.be.

A) LIVE VACCINE

Immunosuppressive therapy in general must be stopped 3 months before vaccination and performed at least 10 days before departure to ensure immunity.

Shortest recommended timeline

Yellow fever (Stamaril®):



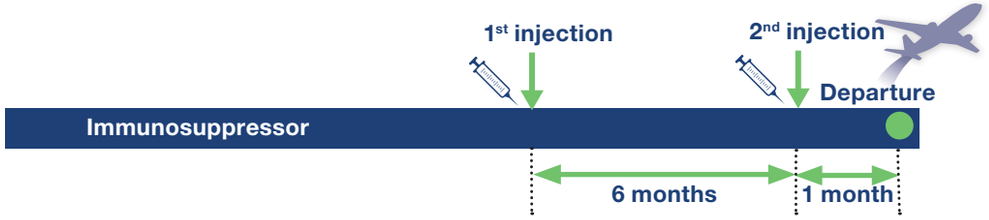
Typhoid fever (Vivotif®): Live vaccine is not used in patients under immunosuppressive therapy. Refer to page 11 for typhoid fever non-live vaccination.

B) NON-LIVE VACCINE

Immunosuppressive therapy can be continued.

Shortest recommended timeline

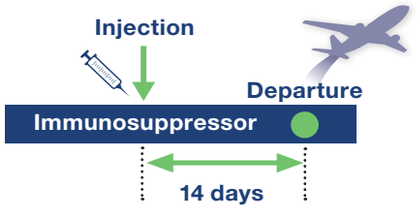
Hepatitis A (Havrix®, Epaxal®, Vaqta®, Twinrix®*): **It is recommended to check immunity 4 to 8 weeks after the 2nd injection in immunosuppressed patients.**



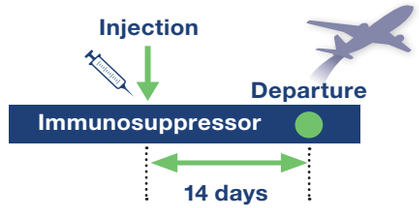
In case lack of time, give 2 injections (double dose) in one time or give injections with 1 month time interval, and do serology. If negative, consult infectious disease/vaccine specialist.

* Twinrix is a combination vaccine for hepatitis A en B and only contains half a dose of hepatitis A.

Meningococcal meningitis type A, C, Y and W135 (Menveo®, Nimenrix®):

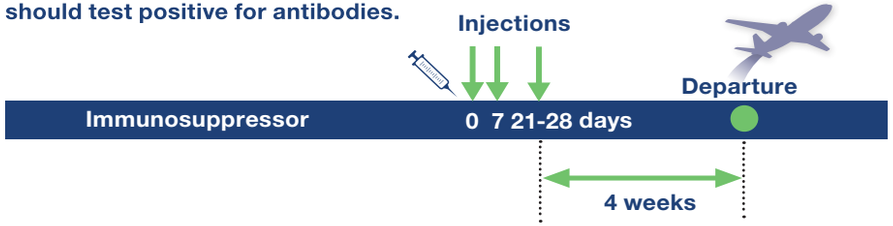


Typhoid fever (Typhim®):



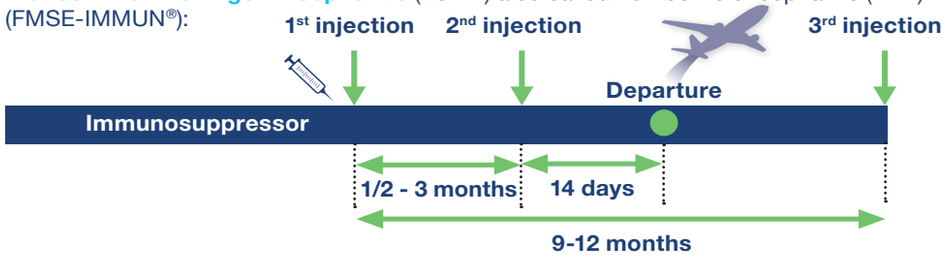
There may be occasions where travelling patients at risk might need to be vaccinated for:

Rabies (Rabipur®, Vaccin Rabique Merieux HDCV®): **It is recommended to check immunity 4 weeks after the 3rd injection in immunosuppressed patients. Patients should test positive for antibodies.**

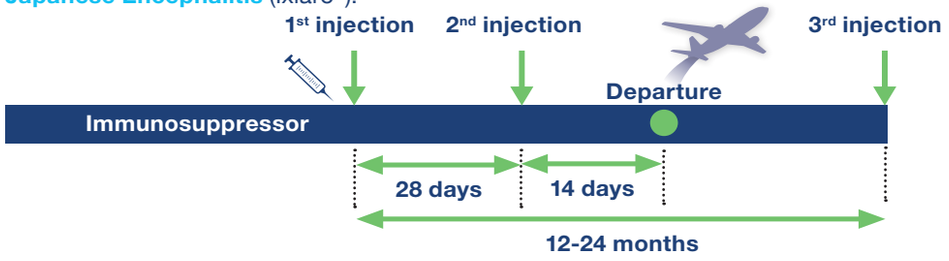


After the pre-exposure vaccination schedule a person is boostable, but not necessarily immune. In case of a bite, a post-exposure schedule comprising 2 injections is always needed.

Frühsommer Meningo-Encephalitis (FSME) also called tick-borne encephalitis (TBE) (FMSE-IMMUN®):



Japanese Encephalitis (Ixiaro®):



Considerations for patients and cohabitants regarding vaccination

1. When cohabitants are vaccinated with a live vaccine, appropriate consideration should be made to ensure that an immunocompromised patient will not be contaminated.

- **Measles, Mumps, Rubella and Varicella:**
  Avoid contact with immunosuppressed patient in case of rash induced by vaccination.
- **Rotavirus:**
  Highly immunocompromised patients should avoid handling diapers of infants who have been vaccinated with rotavirus vaccine for 4 weeks after vaccination.
- **Yellow fever and typhoid fever:**
  No risk or problem to vaccinate cohabitants.

2. When live vaccination of the patient is not possible due to ongoing immunosuppressive therapy, cohabitants should have their immunity checked. In cases where immunity is no longer effective the vaccination scheme should be updated to ensure that the patient is indirectly protected.

- **Measles, Mumps and Rubella**
- **Varicella**
- **Rotavirus** (only in babies before the age of 6 months)

The authors are open for any suggestions on this guide.

ABBVIE SA/NV-BEGEN140265 OCT 2014